

1. (Currently amended) A method for identifying a compound that increases Fhl2 expression or activity in an osteoblast comprising:

- (a) contacting at least one osteoblast with a test compound *in vitro*;
- (b) determining the Fhl2 protein level in the at least one osteoblast;
- (c) comparing said protein level obtained in (b) to the Fhl2 protein level in at least one control osteoblast that has not been contacted with the test compound;
- (d) determining whether the test compound is capable of an action selected from the group consisting of:

- (i) ~~promoting the activity~~increasing Fhl2 expression or activity in ~~of~~ osteoblasts *in vivo*,
  - (ii) ~~modulating the bone formation rate in a non-human test animal~~increasing Fhl2/RunX interaction in osteoblasts *in vivo*, and
  - (iii) promoting the formation of extracellular bone matrix in a non-human test animal, and
  - (iv) combinations thereof, and
- (e) selecting the test compound as a compound that increases Fhl2 expression or activity if the protein level measured in (b) is significantly different from that in the at least one control osteoblast, or if any of the actions in (d) are observed.

2. (Previously presented) The method according to claim 1, wherein said Fhl2 protein level is determined by measuring the level of *Fhl2* expression in the at least one osteoblast.

3. (Previously presented) The method according to claim 1, wherein said Fhl2 protein level is determined by measuring the amount of Fhl2 protein in the nucleus of the at least one osteoblast.

4. (Previously presented) The method according to claim 1, wherein said Fhl2 protein level is determined by determining the level of interaction between Fhl2 protein and Runx2 protein in the osteoblast(s).

5. (Previously presented) The method according to claim 1, wherein the at least one osteoblast is selected from the group consisting of primary osteoblasts, MC3T3-E1 cells, ROS17 cells and U2-OS cells.

6. (Previously presented) A method for preparing a compound that is useful in the treatment of a bone disease, comprising:

- (a) identifying a compound by a method according to claim 1; and
- (b) synthesizing the compound.

7. (Withdrawn) A compound that is useful in the treatment of a bone disease wherein the compound is capable of an activity selected from the group consisting of promoting osteoblast activity by enhancing the expression of the *Fhl2* gene, promoting the translocation of Fhl2 protein in the nucleus, modulating the interaction between Fhl2 protein and Runx2 protein, and combinations thereof.

8. (Withdrawn) A compound according to claim 7 wherein the compound is capable of enhancing signals mediated by Rho proteins.

9. (Withdrawn) A method for the treatment of a bone disease, the method comprising:

administering a therapeutically effective amount of a medicament comprising an *Fhl2* nucleic acid selected from the group consisting of:

- (a) polynucleotides comprising the sequence as shown in SEQ ID NO:1;
- (b) polynucleotides comprising a sequence which has an identity of at least 50% to the sequence as shown in SEQ ID NO:1;
- (c) polynucleotides hybridizing to the sequence as shown in SEQ ID NO:1 under stringent conditions;
- (d) polynucleotides comprising a sequence which encodes a polypeptide having an amino acid sequence as shown in SEQ ID NO:2; and
- (e) polynucleotides comprising a sequence which encodes a polypeptide having an amino acid sequence which has an identity of at least 70% to the amino acid sequence as

shown in SEQ ID NO:2.

10. (Withdrawn) The method according to claim 9, wherein the *Fhl2* nucleic acid is a polynucleotide encoding a polypeptide having an amino acid sequence as shown in SEQ ID NO:2.

11. (Withdrawn) The method according to claim 9 wherein the *Fhl2* nucleic acid is a polynucleotide comprising the sequence as shown in SEQ ID NO:1.

12. (Withdrawn) The method according to claim 9, wherein the bone disease is characterized by a decreased bone mass relative to that of non-diseased bone.

13. (Withdrawn) The method according to claim 9, wherein the bone disease is osteoporosis.

14. (Withdrawn) The method according to claim 9, wherein the *Fhl2* nucleic acid is overexpressed in osteoblasts.

15. (Withdrawn) A method of diagnosing a bone disease, comprising  
(a) determining *in vitro* the level of expression of the *Fhl2* gene in tissue from an individual; and  
(b) comparing the level determined in (a) to the level of expression of the *Fhl2* gene in control tissue;  
so that if the level determined in (a) is lower than that of the control, the individual is diagnosed as exhibiting the bone disease.

16. (Withdrawn) A method according to claim 15 wherein the bone disease is osteoporosis.

17. (Withdrawn) A method for developing a medicament useful for the treatment of bone diseases comprising

a) administering a test compound to a transgenic non-human animal having a decreased level of expression of the Fhl2 gene relative to that of the corresponding wild-type animal,

b) determining osteoblast activity,

c) comparing the activity determined in (b) to the osteoblast activity in a control animal that has not been contacted with the test compound, and

d) selecting the test compound as the medicament useful for the treatment of bone diseases if the activity measured in (b) is significantly different from that in the control animal.

18. (Withdrawn) The method according to claim 17, wherein the transgenic non-human animal is a knockout mouse.

19. (Withdrawn) A method for identifying a compound that promotes the activity of osteoblasts, comprising:

(a) administering a test compound to a transgenic non-human animal having a decreased level of expression of the Fhl2 gene relative to that of the corresponding wild-type animal;

(b) determining an activity of the Fhl2 gene or Fhl2 protein;

(c) comparing the activity determined in (b) to the activity of the Fhl2 gene or Fhl2 protein in a control animal that has not been contacted with the test compound; and

(d) selecting the test compound if the activity measured in (b) is significantly different from that in the control animal.

20. (Cancelled)